immunotherapies like anti-PD1, cancer vaccines, monoclonal antibodies (mAbs), and even CAR-T cells. Subgroup 3 MB is the worst threatening subtype that poorly responds to treatment. Interestingly, our data showed that the HLX gene, a transcription factor that regulates cell growth, is highly expressed in G3-MB and associated with poor prognosis. The siRNA-HLX inhibited tumor growth in vitro and in vivo and promisingly showed long survival in the immunocompetent mouse model. We developed CAR-T-Exosomes that can pass brain-blood barriers (BBB) and deliver therapeutic siRNA to the brain tumor. Further analysis revealed that CAR-T-Exosomes contain T cell cytotoxicity materials that can destroy tumor cells and induce anti-tumor immune response. Promisingly, the expression of HLX was significantly inhibited in the tumor cells and the anti-tumor immune response was enhanced. CAR-T-Exosomes have high safety and can induce anti-tumor response without stimulation of immunotoxicity side effects like cytokine release syndrome (CRS). In this study, we are highlighting anti-EPHA2-CAR-Exosomes as a highly specific type of tumor CAR-T-Exos immunotherapy due to a very low expression of EPHA2 in normal cells and overexpression in medulloblastoma, particularly G3-MB. Therefore, we speculate significant inhibition of tumor growth and activation of CTL effector cells in the tumor microenvironment. This study provides a new biological technique for delivering tumor suppressor RNAs and developing specific anti-tumor immune responses. Indeed, the promising safety of anti-EPHA2-CAR-T cell exosomes compared to cell-based immunotherapy.

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MDB-50. CAR-T CELL-DERIVED EXOSOMES LOADED WITH THERAPEUTIC siRNA IS A PROMISING TECHNIQUE IN THE TREATMENT OF SUBGROUP 3 MEDULLOBLASTOMA
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Medulloblastoma (MB) is a childhood life-threatening tumor that occurs in the cerebellum. This tumor showed resistance against several types of